

found in the specification at page 4, lines 8-10. Support for new claim 15 can be found in Figure 7. Support for new claim 16 can be found in original claims 1 and 9. An **"Appendix of Pending Claims"** is attached for the Examiner's convenience.

Applicants note that cancellation of the claims to the non-elected inventions does not change inventorship of the present invention.

In addition, Applicants assume that the claims to Group I are 1-3 and 9, not 1-3 and 10. Claim 9 addresses recovering a non-naturally occurring TNF- α protein from a host cell which would be appropriately classified in class 530, subclass 350. Claim 10, on the other hand, is drawn to a pharmaceutical composition classified in class 514, subclass 2, which the Examiner has restricted to Group III. Thus, Applicants elect Group I as represented by claims 1-3 and newly added claim 14 which is an independent claim that discloses the subject matter found in original claim 9.

Corrected Sequence Listing and Request for Amendment to Drawing

Applicants have recently identified an obvious mistake in the sequence listing in that the sequences of Figure 7 were inadvertently omitted from the previously filed sequence listing and enclose herewith a corrected sequence listing to include those sequences. This omission is clearly a clerical error and not new material as the specific mutant sequences are disclosed in the figure and the description thereof.

In compliance with 37 C.F.R. § 1.821(d), the specification and claims have been amended to include the corrected Sequence Listing and proper reference to the sequences therein.

Applicants submit that these amendments are not new matter and request their entry. The amendments are made in adherence with 37 C.F.R. §§ 1.821-1.825. This amendment is accompanied by a floppy disk containing the above named sequence, SEQUENCE ID NUMBERS 1-30, in computer readable form (CRF), and a paper copy of the sequence information. The computer readable sequence listing was prepared through use of the software program "PatentIn" provided by the PTO. The information contained in the computer readable disk is identical to that of the paper copy. This amendment contains no new matter. Applicant submits that this amendment, the accompanying computer readable

sequence listing, and the paper copy thereof serve to place this application in a condition of adherence to the rules 37 C.F.R. §§ 1.821-1.825.

Further, in compliance with 37 C.F.R. § 1.121(d), Applicants enclose herewith a revised formal drawing of Figure 7 which has been amended to include sequence identifiers and a copy of the figure with the requested amendments shown in red.

Attached hereto is a marked up version of the changes made to the claims and specification by the current amendment. The attached page is captioned "**Version with Markings to Show Changes Made.**"

The Examiner is invited to contact the undersigned at (415) 781-1989 if any issues may be resolved in that manner.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

Paragraph beginning at page 3, line 24, has been amended as follows:

-- Figure 7 depicts the position and the amino acid changes in the TNF- α mutants (SEQ ID NOS:9-30). --

Paragraph beginning at page 28, line 24, has been amended as follows:

-- Preferred amino acids for each position, including the human TNF- α residues, are shown in Figure 7 (SEQ ID NOS:9-30). Thus, for example, at position 143, preferred amino acids are Glu, Asn, Gln, Ser, Arg, and Lys; etc. --

On page 61, immediately preceding the heading "CLAIMS," the previously filed Sequence Listing was deleted in its entirety and replaced by the enclosed 23-page text entitled "SEQUENCE LISTING".

In the claims:

Claims 4-9, and 10-12 have been cancelled.

Claim 1 has been amended as follows:

1. (Amended) A non-naturally occurring variant TNF- α protein comprising an amino acid sequence that has at least one amino acid substitution as compared to the wild-type TNF- α sequence, wherein said variant TNF- α protein will [preferentially] interact with the wild-type TNF- α to form mixed trimers incapable of activating receptor signaling.

APPENDIX OF PENDING CLAIMS

1. (Amended) A non-naturally occurring variant TNF- α protein comprising an amino acid sequence that has at least one amino acid substitution as compared to the wild-type TNF- α sequence, wherein said variant TNF- α protein will interact with the wild-type TNF- α to form mixed trimers incapable of activating receptor signaling.
2. A non-naturally occurring TNF- α protein according to claim 1 wherein said TNF- α protein has from 3 to 5 amino acid substitutions as compared to wild-type TNF- α sequence.
3. The non-naturally occurring TNF- α protein according to claim 1, wherein said substitutions are selected from the group of substitutions consisting of K112D, Y115T, D143K, D143R, and Y115I.
13. (New) The non-naturally occurring TNF- α protein according to claim 3, wherein said substitution consists of Y115T (SEQ ID NO:20).
14. (New) The non-naturally occurring TNF- α protein according to claim 1, wherein said substitutions are selected from amino acid residues at positions 21, 30, 31, 32, 33, 35, 65, 66, 67, 111, 112, 115, 140, 143, 144, 145, 146 and 147.
15. (New) The non-naturally occurring TNF- α protein according to claim 14, wherein said substitutions are selected from the group of substitutions consisting of D143E, D143N, D143S, A145R, A145K, A145E, E146K, E146R and A84V.
16. (New) A method of recovering a non-naturally occurring variant TNF- α protein comprising an amino acid sequence that has at least one amino acid substitution as compared to the wild-type TNF- α sequence, wherein said variant TNF- α protein will preferentially interact with the wild-type TNF- α to form mixed trimers incapable of activating receptor signaling, from a host cell.